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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/758,335	01/15/2004	Seth J. Orlow	0291472.124US2	6410

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WILMERHALE/BOSTON
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BOSTON, MA 02109

EXAMINER	
ANDERSON, JAMES D	

ART UNIT	PAPER NUMBER
1614	

NOTIFICATION DATE	DELIVERY MODE
02/27/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/758,335	ORLOW ET AL.	
	Examiner	Art Unit	
	JAMES D. ANDERSON	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 December 2008*.

2a)☐ This action is FINAL. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *56,69,78 and 79* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *56,69,78 and 79* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/14/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

Applicants' response and amendments to the claims, filed 12/16/2008, are acknowledged and entered. Claims 56, 69, 78, and 79 are pending and under examination.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/16/2008 has been entered.

Allowable Subject Matter

The indicated allowability of claim 69 is withdrawn in view of the newly discovered reference(s) to the unpredictability of forming "solvates" of organic compounds (Vippagunta, Adv. Drug Del. Rev., Vol. 48, (2001), pp. 3-26). Rejections based on the newly cited reference(s) follow.

Information Disclosure Statement

Receipt is acknowledged of the Information Disclosure Statement filed 8/14/288. The Examiner has considered the references cited therein to the extent that each is a proper citation. Please see the attached USPTO Form 1449.

Claim Rejections - 35 USC § 112 – 2nd Paragraph – New Grounds of Rejection

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 56, 69, 78, and 79 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which

applicant regards as the invention. Independent claims 56 and 69 recite "topical administration" or "contacting the skin" with one or more compounds selected from the group consisting of (II), (III), (IV), (V), (VI), (VII), (VIII) "and a pharmaceutically acceptable salt or solvate thereof". The claims are unclear with respect to whether "a pharmaceutically acceptable salt or solvate thereof" refers only to a pharmaceutically acceptable salt or solvate of compound (VIII) or to a pharmaceutically acceptable salt or solvate of the other compounds in the claim as well. In the absence of a comma between structure (VIII) and "a pharmaceutically acceptable salt or solvate thereof", the claims could be interpreted to only encompass a salt of solvate of compound (VIII).

In addition, the meaning of "...and a pharmaceutically acceptable salt or solvate thereof" is unclear. It is not apparent whether it is Applicant's intent that the Markush group recited in the claims be limited to the selection of compound (II), (III), (IV), (V), (VI), (VII), (VIII); and that such a selected compound is administered with a pharmaceutically acceptable salt or solvate of the selected compound, or whether a pharmaceutically acceptable salt or solvate "thereof" is an additional option in the selection of a compound for administration (i.e., an option is to selected a compound of formula (II), (III), (IV), (V), (VI), (VII), (VIII), or "a pharmaceutically acceptable salt or solvate thereof").

The Examiner suggests amending claims 56 and 69 to clarify that "a pharmaceutically acceptable salt or solvate thereof" is an additional group in the recited Markush group, e.g., by placing a comma between the last structure (VIII) and "a pharmaceutically acceptable salt or solvate thereof" and by replacing "and" with "or".

Claim Rejections - 35 USC § 112 – 1st Paragraph – New Grounds of Rejection

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 78 and 79 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is withdrawn in light of Applicant's amendments.

Claims 56, 69, 78, and 79 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for administering a compound of formula (II), (III), (IV), (V), (VI), (VII), (VIII), or pharmaceutically acceptable salts thereof, does not reasonably provide enablement for administering a "solvate" of the claimed compounds. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. This is a scope of enablement rejection.

The following factors have been considered in the determination of an enabling disclosure:

(1) The breadth of the claims;

(2) The amount of direction or guidance presented;

(3) The state of the prior art;

(4) The relative skill of those in the art;

(5) The predictability or unpredictability of the art;

(6) The quantity of experimentation necessary;

[See *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Int., 1986); also *In re Wands*, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)].

The breadth of the claims: Claims 56 and 69 and dependent claims thereon recite administration of a "solvate" of compounds represented by formulas (II), (III), (IV), (V), (VI), (VII), (VIII). The term "solvate" is known in the art to cover various forms of the same compound at different proportions of water or solvents. Thus, the scopes of the above claims are broad.

The amount of direction or guidance presented: Although the specification discloses that administration of a "solvate" of a compound of formula (II), (III), (IV), (V), (VI), (VII), or (VIII) is within the scope of the invention, it does not provide a single working example for making a solvate. There is no guidance on what proportion of water or solvent to use for obtaining a "solvate". Thus, the specification fails to provide sufficient enablement for making or using a "solvate" of the claimed compounds.

The state of the prior art: Although it is not unusual to expect a "solvate" of a compound, the process for selecting and forming a hydrate or solvate is not standard for all

drugs. For the claimed compounds, there is no reference teaching any possible solvate. Thus, the state of the prior art does not support the broad scopes of the above claims. Furthermore, the teaching of Vippagunta (Adv. Drug Del. Rev., Vol. 48, (2001), pp. 3-26) flatly states on page 18, section 3.4 the following:

> "Predicting the formation of solvates or hydrates of a compound...is complex and difficult."

Thus, the state of the prior art does not support the broad scope of the above claims.

The relative skill of those in the art: Even with the advanced training, the skilled clinician would have to engage in extensive research to select and make a "solvate" for each compound recited in the claims, with no expectation of success.

The predictability or unpredictability of the art & The quantity of experimentation necessary: The process of making a "solvate" is quite unpredictable because it is not possible to predict, a priori, whether solid solutions will form and at what stoichiometry proportion (*i.e*, one, two, or half a molecule of solvent added per molecule of host). Thus, with such a limited teaching from the specification and the art, the skilled chemist would have to engage in undue experimentation, with no reasonable expectation of success, to make a "solvate" of compounds represented by formula in the above claims. In fact, there is no evidence in the art that solvates of the claimed compounds even exist.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of claim 56 under 35 U.S.C. 102(b) as being anticipated by Kagan, is withdrawn in light of Applicants' amendments.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JAMES D. ANDERSON whose telephone number is (571)272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/James D Anderson/
Examiner, Art Unit 1614

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614